

REMARKS

Entry of the foregoing prior to examination on the merits in this 37 C.F.R.

§ 1.53(b) continuation of Appln. No. 09/859,392 filed on May 18, 2001, now abandoned, is respectfully requested.

Upon entry of this amendment, Claims 1, 2, 5-7, 9-11, 13-15, 17-19, 21, 38, 39 and 41-69 will be in this application. Claims 3, 4, 8, 12, 16, 20, 22-37 and 40 have been canceled and Claims 45-69 have been added.

In order to advance prosecution of the application, applicants have amended their claims in light of the Official Action issued by Examiner Gollamudi on March 21, 2003 in the parent application and wish to present a number of remarks regarding same. Claims 1-44 of this application as originally filed corresponded to Claims 16-59, respectively, of the parent application as examined in the March 21, 2003 Official Action therein.

A provisional double patenting rejection of the composition claims of the parent application was made therein over the composition claim of copending Appln. No. 09/859,384. At the present time, no composition claim has yet been allowed in Appln. No. 09/859,384. In fact, Appln. No. 09/859,384 was recently abandoned in favor of a continuation application, Appln. No. 10/702,736, filed November 7, 2003 [Attorney Docket No. 016800-652]. It is therefore requested that the double patenting rejection be held in abeyance until such time as a composition claim is found to be allowable in one of the applications, at which time applicants will take appropriate action in the other

application by deleting or amending the overlapping claims, or filing an appropriate terminal disclaimer therein.

A number of 35 U.S.C. § 112, second paragraph, rejections were made in the March 21, 2003 Official Action. It is believed that all of the claims now in the application are free of these rejections. The claims now use Markush language in connection with the bioaffecting agents and the types of manganese, and the word "natural" does not appear in the amended claims. Further, the claims which the Examiner considered redundant in the parent, i.e. parent Claims 27, 35 and 43, have no counterparts in the amended claims. Thus, the amended claims are free of the §112 rejections made in the parent.

All of parent Claims 16-59 were rejected under 35 U.S.C. § 102(b) as anticipated by EP 0424033 (Okaya et al.). The present claims are free of this rejection. Okaya et al. disclose a topical composition comprising Mn-SOD and a manganese salt for combating skin-roughening. Applicants' Claims 1, 2, 5-7, 9-11, 13-15, 17-19, 21, 38, 39 and 41-46 now use "consisting of" language to define the composition applied. Such language is closed and does not allow for the presence of anything not recited in the claims. All of applicants' recited ingredients are disclosed in the specification; see, in particular paragraphs [0044] through [0054]. While some of the ingredients recited are in broad categories, for example, "retinoids" and "emulsifiers", none of them includes manganese-containing superoxide dismutase ("Mn-SOD") or chemically-modified manganese-containing superoxide dismutase ("modified Mn-SOD"), an essential ingredient in Okaya et al.'s composition. Therefore, applicants believes these claims are free of the §102(b)

rejection based on Okaya et al. As to the remaining claims, that is, Claims 47-69, Claim 47 and its dependent claims recite that the composition comprises at least one form of manganese selected from the group consisting of organic salts of manganese, inorganic salts of manganese, manganese-rich plant extracts and manganese-rich microorganism extracts, and further that said at least one form of manganese is the sole active ingredient for treating skin pallor resulting from stress in the composition. These claims thus exclude use of Okaya et al.'s composition from their scope, first because Mn-SOD/modified Mn-SOD is not one of the forms of manganese in the Markush group, and secondly because Mn-SOD/modified Mn-SOD, if it is an active ingredient for treating skin pallor as the Examiner maintains, by inherently performing this function, is excluded by the "sole active ingredient for ..." clause in these claims. Similar language in Claims 48 and 49 and their dependent claims likewise avoids the Okaya et al. reference.

Applicants would like to comment here in response to the Examiner's position that the cause of the condition does not hold patentable distinction unless it imparts a different characteristics on the condition than that known in the art. This is not in point. It is well-established that in the case of method claims, the invention can reside in the selection of a new and unobvious population to which a composition is administered. Thus, totally apart from any differences in the composition applied, applicants' method as claimed in all of their method claims comprises administering the composition to an individual subject afflicted with skin pallor resulting from stress. Without applicants' teaching that the instant compositions can combat skin pallor resulting from stress, one of ordinary skill would not

expect that, because Okaya's composition combats rough skin, it could be used to combat paleness of skin in persons having skin pallor caused by stress, much less that the different composition of applicants' claims, which does not contain Okaya et al.'s essential Mn-SOD, would be expected to have such a use. Furthermore, it is quite apparent from Okaya et al. that their aim was to provide a composition of Mn-SOD/modified Mn-SOD with improved potential against skin-roughening by maintaining the stability of the enzyme activity, and this they accomplished by adding a manganese salt. They clearly attribute the anti-skin roughening properties of their composition to Mn-SOD/modified Mn-SOD; therefore, one of ordinary skill would not be led to make a composition free of Mn-SOD/modified Mn-SOD and to use it to treat a different population not even alluded to by Okaya et al., i.e. individuals afflicted with skin pallor resulting from stress. The Examiner is using applicants' own teachings to aid here in rejecting applicants' invention, which is impermissible. As noted in paragraph [0010] of the present application, heretofore no link had been established between the calcium channels of the subcutaneous vascular tissue, manganese and the pallor following a stress episode, and accordingly, it was never considered to treat these phenomena by influencing the calcium channels, in particular via manganese.

In the March 21, 2003 Official Action in the parent, Claims 16, 18, 23, 27-28, 39 and 43-44 were rejected under 35 U.S.C. § 102(b) as anticipated by JP403017004A. The present claims are free of this rejection. The reference discloses a cosmetic based on an infrared-radiative ceramic powder containing oxides such as zirconia, titanium dioxide,

alumina and/or silica, to which further oxides of manganese, iron, cobalt etc. are added.

The powder emits infrared rays which internally warm the body to dilate the fine blood vessels and thus improve blood circulation to prevent roughness or dryness. The invention of this reference absolutely requires the presence of metallic oxides. Manganese oxide is not one of the forms of manganese recited in applicants' claims. It is not an organic or inorganic salt of manganese; a salt is the compound formed when the hydrogen of an acid is replaced with a metal, in this case manganese. Thus, an organic salt of manganese is formed when the hydrogen of an organic acid is replaced with manganese, for example, manganese carbonate, MnCO_3 , is the manganese salt of carbonic acid, H_2CO_3 ; an inorganic salt of manganese is formed when the hydrogen of an inorganic acid is replaced with manganese, for example, manganese chloride, MnCl_2 , is the manganese salt of hydrochloric acid, HCl . An oxide of manganese, MnO or MnO_2 , is clearly not formed by replacing the hydrogen of an acid with manganese; it is not an organic or inorganic manganese salt. Equally clearly, it is not a manganese-rich plant or microorganism extract. Thus, it is not one of the forms of manganese recited in the claims now in this application. And, as already explained, the other language of the current claims makes it clear that they are not open to the inclusion of an oxide of manganese for the same reasons that they are not open to the inclusion of Mn-SOD or modified Mn-SOD.

Claims 16-25, 27-33, 35-41, 43-49, 51-57 and 59 of the parent were rejected in the parent under 35 U.S.C. § 102(b) as being anticipated by Patrick U.S. Patent No. 5,496,827. This rejection too cannot be maintained against the present claims.

The Examiner's summary of the teachings of Patrick neglects to point out that Patrick's topical compositions contain, as an essential ingredient, methyl nicotinate. In column 2 of the patent, Patrick teaches that methyl nicotinate is an obscure form of Vitamin B-3. Patrick teaches in column 1 that most vitamins supply Vitamin B-3 as niacinamide, and that niacinamide itself causes release of histamine and causes niacin flush, in which the skin becomes quite red (also column 1). Patrick teaches in column 2 that methyl nicotinate has the power to penetrate the skin topically and limit the niacin flush to a specific area. It also induces rapid transdermal intake of other B vitamins and trace elements in as short a time as 15 seconds. The effects referred to in column 8, which Patrick clearly indicates result from the release of histamine, would thus be understood by one skilled in the art to be the effects of Patrick's essential methyl nicotinate, not of the trace elements of selenium, manganese, chromium or zinc or other vitamins whose transdermal delivery is facilitated by the methyl nicotinate (paragraph bridging columns 5 and 6). There is not a scintilla of a suggestion in Patrick that his lotion would cause hands to be pink because of the presence of anything other than methyl nicotinate. Further, applicants' present claims do not allow for the inclusion of Patrick's essential methyl nicotinate, because of the "consisting of" or "sole active ingredient" language used herein.

In the March 21, 2003 Official Action in the parent, all of the claims were rejected under 35 U.S.C. § 103(a) as unpatentable over Breton et al. U.S. Patent No. 5,900,257. It is submitted that the claims now in this application are free of this rejection.

Breton et al. teach that a wide variety of mammalian disorders, especially of the skin, hair and mucous membranes, result from an excess in the synthesis or release of substance P, and that compositions comprising an effective substance P antagonist amount of at least one salt of yttrium, lanthanum, cerium, praseodymium, neodymium, promethium, samarium, europium, gadolinium, terbium, dysprosium, holmium, erbium, thulium, ytterbium, lutetium, tin, manganese, or mixture thereof, in a cosmetically/pharmaceutically acceptable medium therefor, can be used in the treatment of those conditions. Among the many conditions disclosed by Breton et al. as susceptible to treatment with substance P antagonists are intestinal spasticities and vasospastic disorders. These particular conditions are thus characterized by spasms, not simply contractions. Indeed, the '257 patent focuses on disorders related to an excess of substance P, which is known as a polypeptide of the central and peripheral nervous system involved in the transmission of pain. Vasospastic disorders (migraine, Raynaud's disease) are cited in column 1 as an example of disorders associated with an excess of substance P and the invention proposes to use a substance P antagonist (salt of yttrium etc.) to inhibit the sensitive troubles associated with an excess of substance P. There is no teaching of any other effect of the substance P antagonist, in particular on the diseases as such.

In contrast, the present invention focuses on inhibiting the vasoconstriction induced by physiological stress of dermal capillaries by use of manganese salts. This vasoconstriction is mediated by a Ca^{+2} dependent release of noradrenalin via the sympathetic nervous system. Furthermore, as pointed out previously, and as noted in

paragraph [0010] of the instant specification, prior to applicants' invention, no link had been established between the calcium channels of the subcutaneous vascular tissue, manganese and the pallor following a stress episode, and accordingly, it was never considered to treat these phenomena by influencing the calcium channels, in particular via manganese.

Still further, one of the objects of Breton et al. is to treat inflammatory and allergic diseases as well as intolerant skin, which reacts to irritants, for example, by reddening. A substance P antagonist useful in treating such conditions, which would reduce redness, would therefore not be considered by one of ordinary skill to be likely to be useful in treating paleness due to stress. Skin pallor is indeed the antithesis of skin reddening. Moreover, Breton et al. teach eighteen different metals as substance P antagonists. There is nothing in Breton et al. which would motivate one of ordinary skill to first select salts of manganese from the numerous metals disclosed as substance P antagonists and then find manganese salts useful in treating skin pallor resulting from stress, a condition undisclosed by Breton et al. Still further, applicants again point out that their claims are directed to treatment of a very specific population undisclosed and unsuggested by Breton et al., i.e. individuals afflicted with skin pallor resulting from stress; the Examiner cannot ignore this claim language in determining patentability herein. This recitation of the individuals to be treated defines and identifies a specific group of individuals which is not even specified among the numerous groups of individuals afflicted with the many different skin conditions

disclosed by Breton et al. Clearly, the present invention is patentable over the Breton et al. patent.

Applicants further point out that many of their dependent claims are limited to specific percentage ranges of manganese salts; these claims have an upper limit of 1 % as shown in the instant Examples. When the '257 patent uses a manganese salt, the amount is 5 % or 15 % (Examples 8 and 3, respectively). Applicants' upper limit in the claims reciting percentages is thus 5 to 15 times lower than the amounts used in the '257 patent. Clearly, there is no suggestion that the small amounts recited by applicants would efficiently relax subcutaneous capillaries. Thus, the claims specifying percentages are particularly unobvious in light of the '257 patent.

In view of the foregoing, it is submitted that the claims now in this application are free of all record rejections. Favorable action in the form of a Notice of Allowance is believed to be next in order and is earnestly solicited.

Respectfully submitted,

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Date: February 17, 2004

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